

## REMARKS

Claims 1, 5-13, 15-21, and 23-24 are pending in this application. Claims 15-21 were previously withdrawn from consideration, claims 2 and 22 were previously cancelled, and claims 3, 4, and 14 are herein cancelled. Claims 1 and 13 have been amended. Applicant respectfully requests entry of the foregoing timely presented amendments.

### I. Rejection under 35 U.S.C. § 112, ¶ 1

The Examiner has rejected claims 1, 3, 5-13, and 24 under 35 U.S.C. § 112, first paragraph, because the specification allegedly "does not disclose a genus of variants for cyclosporin derivatives prepared via polyanion intermediates." [Mar. 2, 2006, Office Action at 3]. Specifically, the Examiner argues that the specification allegedly "does not describe preparing any other cyclosporin derivatives, which are not cyclosporin A derivatives and do not contain sarcosine at 3 position," and "does not disclose any cyclosporin derivatives having various substituents at different positions." [*Id.*]. The Examiner argues that the skilled artisan "would not know at what position the substituent occurs in the cyclosporin derivatives, and whether the cyclosporin derivatives are functional," because of the alleged lack of guidance on how to prepare cyclosporin polyanions at different positions. [*Id.* at 3-4]. The Examiner concludes that the Applicant has allegedly failed to sufficiently describe the claimed invention because of the "lack of description on the structures of various cyclosporin polyanions, and the lack of representative species as encompassed by the claims." [*Id.* at 4].

Applicant respectfully traverses this rejection and submits that the skilled artisan would clearly understand how to prepare cyclosporin derivatives, other than cyclosporin A derivatives, with substituents, other than sarcosine, at the 3 position. The Examiner has conceded that the specification "indicates the present invention provides a process of preparing a polyanion by treatment of a cyclosporin with a hexamethyldisilazane metal salt, optionally in the presence of a metal halide, which results in cyclosporin derivatives modified at the 3-position with a markedly improved yield and the reaction is carried out at a higher temperature and with lower excess of electrophile (pages 2-3)." [*Id.* at 3]. The Examiner has also conceded that the "specification discloses cyclosporin A derivatives having various substituents at [the] 3 position prepared by reacting a polyanion containing an anion at sarcosine of 3 position with an electrophilic agent (Examples 1-4)."

The Examiner, however, has failed to consider the remainder of the teachings in the specification, which disclose the preparation of the polyanion intermediates and their use to prepare cyclosporin derivatives, other than just cyclosporin A derivatives, with different substituents, other than just sarcosine, at the 3 position. The specification discloses the polyanion intermediates that can be used to prepare the various cyclosporin derivatives. Specifically, the specification identifies the polyanion intermediates of general formula (II) and identifies the possible substituents that the formula may have. [Specification at 3-10]. Although the specification provides examples of the preparation of cyclosporin A derivatives containing sarcosine at the 3 position, the specification discloses on page 10 that the cyclosporin derivatives are not so limited. Indeed, the specification discloses that the polyanion intermediates are

useful in the preparation of cyclosporin derivatives of general formula (IV). [Specification at 10]. Formula (IV) can be other cyclosporin derivatives, not just cyclosporin A derivatives, and  $R_3$  (the substituent at the 3 position) can be a number of different substituents, not just sarcosine. [Specification at 10-16]. Thus, reading this disclosure and taking into account the general knowledge that one would possess in this field, the skilled artisan would readily understand how to prepare polyanion intermediates and use them to prepare cyclosporin derivatives, other than cyclosporin A derivatives, with substituents, other than sarcosine, at the 3 position.

In order to expedite prosecution, however, Applicant has amended claim 1 to incorporate the subject matter previously recited in claim 4; has amended claim 13 to incorporate the subject matter previously recited in claim 14; and has cancelled claim 3. Applicant reserves the right to pursue the subject matter of these cancelled claims in a later continuing application. These amendments obviate the Examiner's rejection and Applicant respectfully requests that the Examiner withdraw this rejection.

## **II. Rejection under 35 U.S.C. § 112, ¶ 2**

The Examiner has rejected claim 14 under § 112, second paragraph, because the claim allegedly recites " $NG_1G_2$  and formula (V), but the claim does not define  $G_1$ ,  $G_2$ , and  $G_3$ ." [*Id.* at 4]. The Examiner also alleges that claim 14 improperly depends from both claims 4 and 13. [*Id.*]. As noted above, Applicant has amended claim 13 to incorporate the subject matter previously recited in claim 14. Applicant has also amended claim 13 to specifically define  $R_1$  to  $R_{11}$  and  $Z_1$  to  $Z_{11}$ , and  $G_1$ ,  $G_2$ , and  $G_3$  as they were originally defined in claims 4 and 14, respectively. Accordingly, this

amendment obviates the Examiner's rejection and Applicant respectfully requests that the Examiner withdraw this rejection.

**III. Objection to Claims 4 and 23**

The Examiner has objected to claims 4 and 23 "because the claims depend from a rejected claim." Applicant has accordingly cancelled claim 4 and, in light of the arguments made above, Applicant respectfully requests that the Examiner withdraw the objection to claim 23.

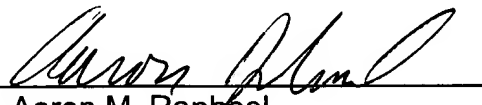
In view of these amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

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By:   
Aaron M. Raphael  
Reg. No. 47,885